

## WHAT IS CLAIMED

1. A stable isolated peptide comprising an amino acid sequence with at least 90% identity to any one of SEQ ID NO:2-6, 8-11 or 14.
2. A stable isolated peptide comprising any one of SEQ ID NO:2-6, 8-11 or 14.
3. The stable isolated peptide of claim 1 or 2 wherein the peptide has a polyproline helix, a short loop region, and an alpha helix, and wherein the peptide folds so that the polyproline helix and the alpha helix hydrophobically interact.
4. The stable isolated peptide of claim 1 or 2 wherein the peptide is more stable than a peptide having SEQ ID NO:1.
5. The stable isolated peptide of claim 1 or 2 wherein the peptide comprises an amino acid sequence with at least 90% identity to SEQ ID NO:11 or 14.
6. A stable isolated peptide comprising SEQ ID NO:11 or 14.
7. The stable isolated peptide of claim 6 wherein the peptide has a polyproline helix, a short loop region, and an alpha helix, and wherein the peptide folds so that the polyproline helix and the alpha helix hydrophobically interact.
8. The stable isolated peptide of claim 6 wherein the peptide is folded and further stabilized by a disulfide bond.
9. The stable isolated peptide of claim 6 wherein the peptide is more stable than a peptide having SEQ ID NO:1.
10. An isolated nucleic acid encoding a stable peptide comprising an amino acid sequence with at least 90% identity to any one of SEQ ID NO:2-6, 8-11 or 14.

11. The isolated nucleic acid of claim 10 wherein the peptide comprises an amino acid sequence with at least 90% identity to any one of SEQ ID NO:11 or 14.

12. An isolated nucleic acid encoding a stable peptide comprising amino acid sequence SEQ ID NO:11 or 14.

13. The nucleic acid of claim 12 wherein the nucleic acid comprises SEQ ID NO:12 or 13.

14. A peptide-based reagent comprising a peptide backbone and an interactive domain, where the peptide backbone comprises an amino acid sequence with at least 90% identity to any one of SEQ ID NO:2-6, 8-11 or 14.

15. A peptide-based reagent comprising a peptide backbone and an interactive domain, where the peptide backbone comprises any one of SEQ ID NO:2-6, 8-11 or 14.

16. The peptide-based reagent of claim 14 or 15 wherein the peptide backbone has a polyproline helix, a short loop region, and an alpha helix, and wherein the peptide backbone folds so that the polyproline helix and the alpha helix hydrophobically interact.

17. The peptide-based reagent of claim 14 or 15 wherein the peptide backbone is more stable than a peptide having SEQ ID NO:1.

18. The peptide-based reagent of claim 14 or 15 wherein the peptide-based reagent is more stable than the peptide backbone without the interactive domain.

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19. The peptide-based reagent of claim 14 or 15 wherein the interactive domain is a binding domain, an inhibitor domain, an antigen-recognizing peptide, a linker, a label, a solid support, or an enzymatic active site.
20. The peptide-based reagent of claim 14 or 15 wherein the interactive domain is a peptide comprising SEQ ID NO:18.
21. The peptide-based reagent of claim 14 or 15 wherein the peptide backbone comprises an amino acid sequence with at least 90% identity to SEQ ID NO:11 or 14.
22. A peptide-based reagent comprising a peptide backbone and an interactive domain, where the peptide backbone comprises SEQ ID NO:11 or 14.
23. The peptide-based reagent of claim 22 wherein the peptide backbone has a polyproline helix, a short loop region, and an alpha helix, and wherein the peptide backbone folds so that the polyproline helix and the alpha helix hydrophobically interact.
24. The peptide-based reagent of claim 22 wherein the peptide backbone is folded and further stabilized by a disulfide bond.
25. The peptide-based reagent of claim 22 wherein the peptide backbone is more stable than a peptide having SEQ ID NO:1.
26. The peptide-based reagent of claim 22 wherein the peptide-based reagent is more stable than the peptide backbone without the interactive domain.
27. The peptide-based reagent of claim 22 wherein the interactive domain is a binding domain, an inhibitor domain, an antigen-recognizing peptide, a linker, a label, a solid support, or an enzymatic active site.

28. The peptide-based reagent of claim 22 wherein the interactive domain is a peptide comprising SEQ ID NO:18.

29. A method comprising:

- (a) defining a search zone comprising a site of interaction on a target protein to which a peptide can interact;
- (b) defining a size for the peptide;
- (c) defining a class of amino acids for each position in the amino acid sequence of the peptide;
- (d) substituting each member of a defined class of amino acids into each position of the amino acid sequence of the peptide sequence to generate an output library file comprising a plurality of output peptide sequences;
- (e) communicating the output library file to a molecular docking program to fit each of the plurality of output peptide sequences to the search zone and to create a target protein-peptide sequence fit score;
- (f) ranking the plurality of output peptides sequences by target protein-peptide sequence fit score; and
- (g) displaying each of the plurality of output peptide sequences and its associated target protein-peptide sequence fit score;

wherein a portion of the plurality of output peptide sequences can stably interact with the target protein.

30. The method of claim 29 wherein the search zone comprises x-, y-, and z-coordinates of each non-hydrogen atoms in the target protein.

31. The method of claim 29 wherein output peptide sequences with higher target protein-peptide sequence fit scores can potentially bind with higher affinity to the target protein.

32. The method of claim 29 that further comprises receiving an input percentage selection to limit the plurality of output peptide sequences to a certain percentage; wherein the input percentage selection is capable of limiting an output library file size and a library complexity.
33. The method of claim 29 wherein each class of amino acids separately comprises any one of genetically encoded L-amino acids, naturally occurring non-genetically encoded L-amino acids, synthetic L-amino acids, D-enantiomers of genetically encoded amino acids, D-enantiomers of naturally occurring non-genetically encoded amino acids, or synthetic D-amino acids.
34. The method of claim 29 wherein each class of amino acids separately comprises any one of hydrophilic amino acids, hydrophobic amino acids, cysteine-like amino acids, acidic amino acids, basic amino acids, polar amino acids, aromatic amino acids, apolar amino acids or aliphatic amino acids.
35. The method of claim 29 wherein the target protein is bovine pancreatic trypsin and one of the output peptide sequence is YKLKY (SEQ ID NO:18).
36. A system for creating peptide sequences, comprising:
  - (a) a processor;
  - (b) a memory coupled to the processor;
  - (c) a display couple to the processor;
  - (d) a make peptide sequence component capable of executing on the processor to generate peptide sequences;
  - (e) an output class component capable of executing on the processor to display each class of amino acid residues used by the make peptide sequence component; and
  - (f) an output peptide sequence component capable of executing on the processor to display peptide sequences.

37. The system as recited in claim 36 wherein the display is a printer.

38. The system as recited in claim 36, wherein the output class component is capable of displaying each class of amino acid residues used by the make peptide sequence component.

39. A machine-accessible medium having associated content capable of directing the machine to perform a method, the method comprising:

- (a) receiving a search zone comprising a plurality of coordinates for atoms in an target site to which a plurality of peptides can bind with varying affinities;
- (b) receiving a peptide length parameter comprising a number of amino acids;
- (c) receiving a defined class of amino acid structures to be analyzed for fitness at each position along the peptide length;
- (d) generating an output library file comprising a plurality of output peptide sequences containing each amino acid from each defined class of amino acid structures at each position along the peptide length;
- (e) sequentially translating and rotating each member of the class of amino acid structures at each position within a peptide relative to the search zone to sequentially create a peptide sequence with a target site-peptide sequence fit score;
- (f) ranking peptide sequences by target site-peptide sequence fit scores; and
- (g) displaying a selected percentage of the target site-peptide sequence fit scores with the associated peptide sequences.

40. The machine-accessible medium as recited in claim 39, further comprising:  
displaying labels for the output peptide sequences.

41. The machine-accessible medium as recited in claim 39, further comprising:  
storing the search zone.

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